Listing of the Claims

The following listing of the claims replaces all other listings and versions of the claims in the application.

1. (***Withdrawn***) A method for determining a T-cell epitope of a protein, wherein said protein is a bone morphogenetic protein (BMP), comprising the steps of:

(a) obtaining from a solution of dendritic cells and a solution of naïve CD4+ and/or CD8+ T-cells from a single human blood source;

(b) differentiating said dendritic cells, in said solution of dendritic cells, to produce a solution of differentiated dendritic cells;

(c) preparing a pepset of peptides from said protein;

(d) combining said solution of differentiated dendritic cells and said naïve CD4+ and/or CD8+ T-cells with said pepset, wherein said pepset comprises said T-cell epitope; and

(e) measuring the proliferation of said T-cells in said step (d).

2. (***Withdrawn***) The method of Claim 1, wherein said protein is selected from the group consisting of BMP-7 and BMP-14.

3. (***Withdrawn***) The method of Claim 1, wherein said pepset comprises a peptide having the sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5.

4. (***Withdrawn***) The method of Claim 1, wherein said pepset comprises a peptide having the sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8.

5. (***Withdrawn***) The method of Claim 1, further comprising the step of modifying said protein to produce a variant protein, wherein said variant protein exhibits an altered immunogenic response as compared to said protein.

6. (***Withdrawn***) A peptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8.

7. (***Currently Amended***) A method of reducing the immunogenicity of a protein, wherein said protein is a bone morphogenetic protein, comprising ~~the steps of:~~

~~(a) identifying at least one T-cell epitope in said protein by~~

~~(i) contacting an adherent monocyte-derived dendritic cell that has been differentiated by exposure to at least one cytokine in vitro, with at least one peptide comprising said T-cell epitope; and~~

~~(ii) contacting said dendritic cell and said peptide with a naïve T-cell, wherein said naïve T-cell has been obtained from the same source as said adherent monocyte-derived dendritic cell, and whereby said T-cell proliferates in response to said peptide; and~~

~~(b)~~ modifying said protein to neutralize ~~said~~ a T-cell epitope to produce a variant protein, such that said variant protein induces less than or substantially equal to the baseline proliferation of ~~said~~ naïve T-cells;

wherein the amino acid sequence of said T-cell epitope is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8.

8. (***Previously Presented***) The method of Claim 7, wherein said T-cell epitope is modified by substituting a portion of the amino acid sequence of said T-cell epitope with an analogous sequence from a homolog of said protein.

9. (***Previously Presented***) The method of Claim 7, wherein said T-cell epitope is modified by substituting the amino acid sequence of said T-cell epitope with a sequence which substantially mimics the major tertiary structure attributes of said T-cell epitope.

10. (***Previously Presented***) The method of Claim 7, wherein said protein is selected from the group consisting of BMP-7 and BMP-14.

11. (***Canceled***)

12. (***Currently Amended***) A method for producing a variant protein having reduced allergenicity comprising the steps of:

~~a) obtaining a naturally-occurring protein, wherein said naturally-occurring protein is a bone morphogenetic protein, and preparing fragments of said naturally-occurring protein;~~

~~b) contacting said fragments of said naturally-occurring protein with a first solution comprising naïve human CD4+ or CD8+ T-cells and differentiated dendritic cells;~~

~~c) identifying an epitope region of said naturally-occurring protein, wherein said identifying comprises measuring the ability of said fragments of said naturally-occurring protein epitope region to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells; and~~

~~d)~~ modifying at least one amino acid in ~~said~~ a T-cell epitope region ~~identified in step c)~~ of a naturally-occurring protein to produce said variant protein; wherein said naturally-occurring protein is a bone morphogenetic protein; and

wherein the amino acid sequence of said T-cell epitope is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7 and SEQ ID NO:8.

13. (***Previously Presented***) The method of Claim 12, further comprising the step of comparing the ability of said fragments of said naturally-occurring protein to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells with the ability of said fragments of said variant protein to stimulate proliferation of said naïve human CD4+ or CD8+ T-cells.

14. (***Previously Presented***) The method of Claim 12, wherein said protein is a bone morphogenetic protein.

15. (***Previously Presented***) The method of Claim 14, wherein said bone morphogenetic protein is selected from the group consisting of BMP-7 and BMP-14.

16. (***Canceled***)